HAEMOPHILUS INFLUENZAE

Invasive Disease

Report Immediately

✓DISEASE AND EPIDEMIOLOGY

Clinical Description:

Invasive disease due to *H. influenzae* may produce various clinical syndromes including meningitis, bacteremia or sepsis, epiglottitis, pneumonia, septic arthritis, osteomyelitis, pericarditis, empyema, and abscesses. Mucosal infections, such as bronchitis, sinusitis and conjunctivitis, and otitis media, can also be caused by *H. influenzae,* but they are considered to be noninvasive disease.

Causative Agent:

Haemophilus influenzae is a small gram-negative coccobacillus that may be either encapsulated (types a–f) or unencapsulated (non-typeable). Non-typable strains are thought to be less virulent than encapsulated strains. *Haemophilus influenza* type b (Hib) is the serotype that requires control measures.

Differential Diagnosis:

Invasive *H. influenzae* can cause pneumonia, bacteremia, or meningitis. The presentation of these diseases is similar to other invasive bacterial diseases such as *Streptococcal pneumoniae* or *Streptococcal pyogenes*.

Laboratory identification:

H. influenzae is typically identified via culture, through blood or CSF samples. All isolates should be sent to the UPHL for serotyping. Labs occasionally use antigen detection methods, but these are not considered confirmatory in the absence of culture positivity.

> **UPHL:** The UPHL serotypes all isolates of *H. influenzae* from clinical laboratories.

Treatment (Hib):

Typical treatment regimens for Hib include cephalosporins and quinolones. Isolate the case until 24 hours after initiating appropriate antimicrobial treatment that eliminates carriage. Currently, only cefotaxime and ceftriaxone are known to eradicate Hib from the nasopharynx when they are used to treat active infection. Therefore, if the patient is treated with ampicillin or chloramphenicol instead, he/she must receive rifampin prophylaxis. Also, note that Hib disease does not necessarily confer immunity to subsequent disease. Immunize as follows:

a. Children with invasive Hib disease at <24 months of age: Immunize according to the age-appropriate schedule for unvaccinated children and as if they had received no prior doses, as disease in this age group does not reliably result in a protective immune response. Begin one month after onset of disease or as soon as possible thereafter.

b. Children with invasive Hib disease at ≥24 months of age: No Hib immunization is necessary, regardless of previous immunization status, because the disease probably induces a protective immune response and second episodes in children this age are rare. However, Hib vaccination is not contraindicated and can be given as a single antigen or as part of a combination vaccine.

Case fatality:

Invasive infections due to *H. influenza* are serious and can be rapidly fatal. As of 2005, 15% of invasive cases were fatal in the U.S.

Reservoir:

Humans are the only known host.

Transmission:

H. influenzae infection is transmitted from person to person by droplet or direct contact with nasopharyngeal secretions of an infected person. The most common portal of entry is the nasopharynx. Newborns can become infected by inhaling amniotic fluid or genital tract secretions containing the organism.

Susceptibility:

The vaccine only confers immunity to one strain: type b. People are uniformly susceptible to other strains of this organism. Disease before the age of 2 does not confer immunity; vaccine is still required.

Incubation period:

The incubation period is unknown, but for invasive disease, may be as short as 2–4 days.

Period of communicability:

If the case is not on antibiotic therapy, disease is communicable as long as organisms are present in the upper respiratory tract, which may be for a prolonged period, even without nasal discharge. If the case is on antibiotic therapy, disease is non-communicable within 24–48 hours after starting effective antibiotic therapy.
The contagious potential of invasive *H. influenzae* disease is considered to be limited. However, certain circumstances, particularly close contact with a case (e.g., in a household, daycare center, or institutional setting), can lead to outbreaks of Hib or direct secondary transmission of the disease. Asymptomatic carriage is known to occur.

Epidemiology:

Haemophilus influenzae type b (Hib) is the only type for which there is a vaccine and for which control measures are considered necessary.

Before the widespread use of Hib conjugate vaccines, Hib was a leading cause of bacterial meningitis in the U.S. among children <5 years of age and a major cause of other life-threatening invasive bacterial disease in this age group. The introduction of Hib

vaccine in 1988 resulted in a 99% decrease in invasive Hib disease in children younger than 5 years of age. Currently, Hib disease occurs primarily in infants too young to have completed a primary series of immunization. Secondary cases may occur in households, daycare centers, and other institutional settings.

Since the introduction of Hib vaccine, the incidence of all infection due to the encapsulated and nontypeable strains combined have decreased. However, *H. influenzae* type f has become the most common serotype causing invasive infections in the U.S. With the reduction of invasive disease due to Hib, the remaining disease is now distributed among the age groups. In Utah, invasive disease due to non-typable strains predominates, and is seen in all age groups.

Unimmunized children, particularly those younger than four years of age, who are in prolonged close contact (such as in a household setting) with a child with invasive Hib disease are at increased risk for invasive Hib disease. Other factors causing predisposition to invasive disease include sickle cell disease, asplenia, HIV infection, certain immunodeficiency syndromes, and malignant neoplasms. Historically, invasive Hib was more common in boys; African American, Alaska Native, Apache and Navajo children; childcare attendees; children living in crowded conditions; and children who were not breastfed.

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Identify clusters or outbreaks of this disease.
- Identify sources of exposure and stop further transmission.
- To identify the emergence of other *H. influenzae* types as causes of invasive disease.
- To monitor Hib vaccine effectiveness, and to assess progress toward disease elimination.

Prevention:

Routine childhood vaccination is the best preventive measure against Hib disease. Good personal hygiene (which consists of proper hand-washing, disposal of used tissues, not sharing eating utensils, etc.) is also important.

Chemoprophylaxis:

Chemoprophylaxis is ONLY indicated for contacts to Hib disease.

Indications and Guidelines for Rifampin Chemoprophylaxis for Contacts of Index Cases of Invasive Haemophilus influenzae Type b (Hib) Disease
Chemoprophylaxis recommended In certain index cases: • Index case, if younger than 2 years of age or member of a household with a susceptible contact and treated with regimens other than cefotaxime or ceftriaxone, chemoprophylaxis usually is provided just before discharge. In certain household situations: • All household contacts (except pregnant women),[1] irrespective of age, in households where at least 1 contact is < 4 years of age and is unimmunized or incompletely immunized. • All household contacts (except pregnant women),[1] irrespective of age, in households where a child is < 12 months of age, if the child has not received the primary series2All household contacts (except pregnant women),[1] irrespective of age, in households with an immunocompromised child, regardless of the child's Hib immunization status In certain child care situations: • Nursery and child care centers contacts, regardless of age when ≥ 2 cases occurred within 60 days.[3,4]
Chemoprophylaxis not recommended In certain individuals: • Pregnant women

In certain household situations:

- Occupants of households with no children < 4 years of age other than the index patient
- Occupants of households when all household contacts 12 to 48 months of age have completed their Hib immunization series[5] and when all household contacts younger than 12 months of age have completed their primary series of Hib immunizations.

In certain child care situations:

- Nursery and child care contacts of 1 index case, especially those contacts > 2 years of age

1. Defined as persons residing with the index patient or nonresidents who spent ≥ 4 hours with the index case for ≥ 5 of the 7 days preceding the day of hospital admission of the index case.

2. The primary series consists of 2-3 doses, depending on the Hib vaccine formulation. See the table below for more details.

3. Only children who are age-appropriately immunized and on rifampin should be permitted to enter the childcare group during the time prophylaxis is given. Children enrolling in the day care center or other setting during the time prophylaxis is given should also receive rifampin, as should supervisory personnel.

4. When a single case has occurred, the advisability of rifampin prophylaxis in exposed child care groups with unimmunized or incompletely immunized children is controversial, but many experts recommend no prophylaxis.

5. Complete immunization is defined as having had ≥ 1 dose of conjugate vaccine at ≥ 15 months of age; 2 doses between 12 and 14 months of age; or a 2- or 3-dose primary series (number of doses required depends on vaccine type and age at initiation) when < 12 months with a booster dose at ≥ 12 months of age.

Vaccine:

Table 1 lists the Hib conjugate vaccines that are currently available. Two combination vaccines that include the Hib conjugate vaccine have been licensed by the FDA following immunogenicity and safety studies (**Table 2**). These combination vaccines decrease the number of injections needed for protection

against vaccine-preventable diseases.

Table 1. Hib conjugate vaccines currently available

Licensed vaccine	Trade name	Manufacturer/Distributor
HbOC	HibTITER®	Wyeth (formerly Lederle-Praxis Laboratories)
PRP-T	ActHIB® OmniHIB®	Aventis Pasteur GlaxoSmithKline
PRP-OMP	PedvaxHIB®	Merck & Company

Table 2. Combination vaccines containing Hib conjugate vaccines

Licensed vaccine	Trade name	Manufacturer/Distributor
PRP-T + DTaP¶	TriHIBit®	Aventis Pasteur
PRP-OMP + HepB	COMVAXTM	Merck & Company

¶ On July 15, 1997, TriHIBit® was licensed for use only for the fourth dose of the DTaP and Hib vaccination series among children 15–18 months of age, to be administered at least 6 months following the third DTP or DTaP dose.

The recommended schedule for Hib conjugate vaccine administration among previously unvaccinated children is given in **Table 3**. Based on the recommended schedule, infants should receive three primary doses of Hib conjugate vaccine with HbOC or PRP-T at ages 2, 4, and 6 months, or two primary doses PRP-OMP at 2 and 4 months. A booster dose should be administered at age 12–15 months with any of the conjugate vaccines. Any type of licensed Hib vaccine may be used interchangeably to complete the series, and the number of doses needed to complete the series is determined by the type of vaccine used (e.g., 4 doses if either HbOC or PRP -T is used at least once)

Table 3. Recommended schedule for Hib conjugate vaccine administration among previously unvaccinated children

Vaccine	Age (months) at first vaccination	Primary series	Booster
HbOC/PRP-T	2–6	3 doses, 2 months apart	12–15 months
	7–11	2 doses, 2 months apart	12–18 months
	12–14	1 dose	2 months later
	15–59	1 dose	NR
PRP-OMP	2–6	2 doses, 2 months apart	12–15 months
	7–11	2 doses, 2 months apart	12–18 months
	12–14	1 dose	2 months later
	15–59	1 dose	NR

NR = Not required

Hib Vaccine Recommendations for Children Not Up-To-Date

Age at Presentation	Previous Vaccination History	Recommended Regimen
7-11 months	0 doses	• 3 doses given with a 1 month minimum interval between dose 1 and dose 2; third dose given at least 2 months after dose 2, at 12-15 months
	1 dose of HbOC, PRP-T or PRP-OMP[1]	• 1 or 2 doses of conjugate vaccine at 7-11 months (depending on age) with a booster dose given at least 2 months later, at 12-15 months

	2 doses of HbOC or PRP-T	• 1 dose of conjugate vaccine at 7-11 months with a booster dose given at least 2 months later, at 12-15 months of age
12-14 months	0 doses	• 2 doses of any conjugate vaccine, with a minimum interval of 2 months [2]
	1 dose before 12 months of HbOC, PRP-T or PRO-OMP[1]	• 2 additional doses of any conjugate vaccine, with a minimum interval of 2 months [2]
	2 doses before 12 months of HbOC, PRP-T or PRP-OMP[1]	• 1 dose of any conjugate vaccine [2]
15-59 months	Any incomplete schedule	• 1 dose of any conjugate vaccine [2]
≥ 60 months	Any incomplete schedule	• 1 or 2 doses of any conjugate vaccine [3]

1. HbOC (HibTITER®), PRP-T (ActHIB®), PRP-OMP (PedvaxHIB®).
2. For children 12-59 months of age with an underlying condition predisposing them to Hib disease (e.g., sickle cell disease, asplenia, HIV infection, AIDS, other immunosuppressive conditions and treatments) who are not immunized or have received only 1 dose of conjugate vaccine before age 12 months, 2 additional doses of licensed conjugate vaccine (separated by 2 months) are recommended. If they have received 2 doses before age 12 months, only 1 dose is recommended. **Note:** Some experts recommend that a reinforcing dose of Hib vaccine should be administered to children receiving treatment for malignancy, to be administered 3 months after completion of treatment.
3. *Children ≥ 60 months of age with an underlying condition predisposing them to Hib disease (e.g. sickle cell disease, asplenia, HIV infection, AIDS, other immunosuppressive conditions and treatments), who are not fully immunized, should receive 1 dose of Hib vaccine. Some experts recommend 2 doses (separated by 1-2 months) for those with HIV infection or IgG2 deficiency.*

Please consult the chapter on *H. influenzae* in the *Red Book* of the American Academy of Pediatrics (AAP) for a full discussion of vaccines, immunization schedules, and special circumstances. For example, children, including those >5 years of age, with underlying conditions predisposing them to Hib disease may need additional doses.

Isolation and quarantine requirements:

Isolation: Cases of invasive H. influenza B disease should be isolated until 24 hours after initiating appropriate antimicrobial treatment.
Hospital: Standard body substance precautions.
Quarantine: Personal surveillance and prophylaxis with an appropriate antimicrobial when indicated by clinical situation of the contact or potential for future transmission. Otherwise, no restrictions.

✓CASE INVESTIGATION

Reporting:

All cases of *H. influenzae* recovered from a sterile site.

Case definition:

Haemophilus influenzae (1997):

Clinical Description

Invasive disease caused by *Haemophilus influenzae* may produce any of several clinical syndromes, including meningitis, bacteremia, epiglottitis, or pneumonia.

Laboratory Criteria

Isolation of *H. influenzae* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid)

Case Classification

Probable: a clinically compatible case with detection of *H. influenzae* type b antigen in CSF
Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Positive antigen test results from urine or serum samples are unreliable for diagnosis of *H. influenzae* disease.

Case Investigation Process:

- Public health needs to immediately determine whether the reported case is due to serotype b. To do this, public health should:
  - Identify the laboratory where the initial testing occurred and
  - Phone them to ensure that the isolate is immediately sent to UPHL for serotyping and
  - Phone UPHL to warn them that an *H. flu* strain is coming and that serotyping needs to occur as soon as possible.
- Cases due to Haemophilus influenzae type b should be immediately investigated:
  - Identify all close contacts (view chemoprophylaxis section for details)
  - Assure that they are provided chemoprophylaxis and vaccine within SEVEN days of hospitalization of the index case.

Outbreaks:
An outbreak will be defined as more than one case of Hib in a 60 day period.

Identification of case contacts:
See Chemoprophylaxis for definition of case contacts.

Case contact management (Hib only):
- Assure that contacts receive chemoprophylaxis. See Chemoprophylaxis for specifics.
- Ensure appropriate immunization of contacts. The number of doses required is determined by the current age of the child and the number, timing, and type of Hib vaccine doses previously received. Unvaccinated and incompletely vaccinated children <5 years of age should be scheduled for completion of the recommended age specific immunization schedule. Infants should be placed on an accelerated schedule using minimum intervals between doses. Unvaccinated high-risk individuals >5 years of age should receive 1 dose.
- Conduct surveillance. Careful observation of exposed contacts, especially children <4 years of age, is essential. Those in whom a febrile illness develops should receive prompt medical attention, regardless of Hib vaccination status.

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